



# Evaluation of Tibial and Median Nerves in Patients with Diabetic Peripheral Neuropathy Using Shear Wave Elastography

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## Abstract

**Background** Diabetes mellitus (DM) leads to diabetic peripheral neuropathy (DPN), a significant complication affecting a large percentage of diabetic patients. Traditional methods like nerve conduction studies have limitations in diagnosing DPN, especially in advanced cases. High-resolution ultrasound has emerged as a valuable tool in enhancing diagnostic accuracy.

**Objective** The aim of the study is to evaluate the efficacy of shear wave elastography (SWE) in assessing DPN, focusing on the tibial and median nerves.

**Materials and Methods** The study involved 100 participants categorized into groups with DPN, DM without DPN, and healthy controls. SWE was performed on the tibial and median nerves, and statistical analysis was conducted to compare the findings among the groups.

**Results** The study found significant increases in SWE values from the normal group to the DM group, and further increases in the DPN group for both tibial and median nerves. Receiver operating characteristic analysis indicated high diagnostic accuracy of SWE in distinguishing DPN from non-DPN cases. Overall, the study suggests that SWE could be a valuable adjunctive imaging tool in diagnosing DPN, offering advantages in terms of sensitivity, specificity, and noninvasiveness.

**Conclusion** The study concludes that SWE of the tibial and median nerves is a noninvasive, sensitive, and specific method for detecting DPN. Combining high-resolution ultrasound with SWE enhances the diagnostic accuracy of DPN.

## Keywords

- ▶ diabetic peripheral neuropathy
- ▶ shear wave elastography
- ▶ tibial nerve
- ▶ median nerve

## Introduction

Diabetes, characterized clinically by elevated blood sugar levels (hyperglycemia), is a chronic condition stemming from either deficiency of insulin (type 1) or resistance to insulin (type 2).

Diabetic peripheral neuropathy (DPN) stands as a significant complication arising from diabetes mellitus (DM).

Approximately 45% of individuals diagnosed with type 2 diabetes and between 54 and 59% of those with type 1 diabetes are affected by peripheral neuropathy.<sup>1</sup>

DPN manifests through diverse symptoms, primarily exhibiting distal sensorimotor polyneuropathy. These symptoms may include neuropathic pain, numbness, and a burning sensation. In severe instances, DPN can lead to critical

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outcomes such as neurogenic joints, ulceration, fractures, ischemic gangrene, and potentially fatal consequences.<sup>2</sup>

DPN is common in diabetes. Diagnosis usually involves symptoms and nerve conduction studies (NCS), but NCS has limitations. It may not detect advanced DPN and can be normal in subclinical cases.<sup>3,4</sup>

Diagnosis of DPN primarily relies on identifying characteristic symptoms, and this diagnosis is typically validated through an NCS.<sup>5</sup> However, conducting electrophysiologic tests in the lower limbs can be time-consuming, and in advanced cases of DPN, action potentials may not be evoked. Additionally, there is a challenge in that NCS results may appear normal in patients with subclinical DPN.<sup>6</sup>

Ultrasound elastography is a noninvasive method for assessing tissue elasticity, with potential applications in diagnosing and monitoring neuromuscular and movement disorders.<sup>7</sup> High-resolution ultrasound has become increasingly valuable in diagnosing DPN, offering a noninvasive means to assess nerve echogenicity and stiffness, thereby enhancing diagnostic accuracy.<sup>8</sup>

The advancement of high-resolution ultrasound technology has significantly enhanced the ability to image lesions with remarkable clarity and precision. Consequently, its clinical application in neuromuscular diseases has rapidly expanded. This expansion is attributed to the ease of use and excellent resolution provided by high-resolution ultrasound, making it a valuable tool in diagnosing and managing various neuromuscular conditions.<sup>9</sup>

Ultrasound imaging offers valuable insights into DPN by providing information on the cross-sectional area (CSA), echogenicity, and inner structure of nerves. These data allow for the assessment of various degrees of DPN. Previous studies have examined the relationship between diabetic neuropathy and the CSA of peripheral nerves using ultrasound, shedding light on the diagnostic and prognostic implications of nerve morphology in DPN.<sup>6</sup>

Shear wave elastography (SWE) is a promising technique widely applied in many organs. SWE shows promise in quantitatively assessing tissue stiffness changes. It achieves this by measuring the speed and propagation pattern of shear waves within the targeted tissue. However, it assumes linear, isotropic tissue behavior, which does not reflect real tissue properties. Standard ultrasonography overlooks effects like wave refraction and reflection, impacting transverse wave propagation imaging. Differences in transverse wave velocities can be substantial, leading to significant reflective impact. Shear wave refraction at tissue boundaries with varying velocities exacerbates these effects.<sup>10</sup>

Until now, very few studies have examined the application of SWE in evaluating DPN, and there is a lack of research on our population. Our study seeks to assess the diagnostic potential of SWE in detecting polyneuropathy in diabetic patients, with a specific focus on the median and tibial nerves.

The primary objective of our study is to determine the efficacy of SWE in assessing DPN. We compared the SWE findings of the tibial and median nerves between patients with DPN, those without DPN, and healthy subjects. Our hypothesis posited that nerves affected by DPN would

exhibit significantly increased stiffness and higher shear wave velocities than those without DPN.

## Materials and Methods

This prospective case-control study involved 100 participants enrolled between January 2023 and March 2024 following approval from the institutional ethics committee. All participants provided signed, written, informed consent in their native language. The study consisted of three groups: the DPN group, comprising 33 patients diagnosed with DPN; the DM group, consisting of 33 patients with DM but without DPN; and the normal group, consisting of 34 healthy controls matched for age and sex. The duration of diabetes in the DM and DPN groups was  $\geq 5$  years.

The inclusion criteria for the study participants were patients with type 2 DM and a confirmed diagnosis of DPN based on NCS (NCS values for DPN—the conduction velocities were  $< 39$  and  $41$  m/s for the median and tibial nerves, respectively) following the revised American Diabetes Association (ADA) diagnostic criteria.<sup>11</sup> Volunteers with no disease, matched for sex and age, who exhibited no clinical signs of DM or DPN were also included. Patients with type 1 diabetes, polyneuropathy due to other causes, a history of leg fracture or surgery, or any autoimmune disease were excluded from the study.

## Statistical Analysis

Collected data were transformed, coded, and entered into Microsoft Excel, then analyzed using SPSS-PC-25. Normality was assessed with the Anderson–Darling test. Parametric data were expressed as mean  $\pm$  standard deviation (SD) or median, compared using *t*-test or Mann–Whitney *U* test. Nonparametric data were presented as number and percentage, analyzed with Pearson's chi-squared test. The receiver operating characteristic (ROC) curves using SWE velocities differentiated between groups, determining cutoff values. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated. A *p*-value less than 0.05 denoted significance.

## Sonographic Technique for Shear Wave Elastography

High-resolution ultrasound and shear wave ultrasound elastography were performed on the tibial and median nerves of both limbs using a Logic P9 ultrasound machine equipped with a high-frequency linear transducer (3–12 MHz). These examinations were conducted by experienced radiologists with over 10 years of expertise.

During the procedure, participants were instructed to assume the supine position, ensuring relaxation of the lower limbs to minimize ankle movement for the tibial nerve examination. For the evaluation of the median nerve, the forearm was positioned supine on a pillow with the elbow and fingers semi-flexed, and the patients were instructed to refrain from moving their fingers throughout the examination.

The tibial and median nerves were assessed in the transverse view, approximately 3 cm above the medial malleolus for the tibial nerve and at the midpoint of the forearm for the

**Table 1** Demographic data among groups

	Normal (n = 34)	DM (n = 33)	DPN (n = 33)	p-value
Age (y)	41.18 ± 12.34	46.3 ± 20.3	50.24 ± 13	0.063
Weight (kg)	72.59 ± 7.44	72.88 ± 7.79	73.06 ± 9.16	0.988
Height (cm)	171.74 ± 6.66	170.42 ± 8.48	168.91 ± 11.04	0.432
BMI (kg/m <sup>2</sup> )	24.59 ± 2.43	24.97 ± 1.67	27.36 ± 2.58	< 0.001
RBS (mg/dL)	174.41 ± 11.69	207.3 ± 33.54	219.94 ± 59.84	< 0.001
HbA1c (mmol/mol)	6.11 ± 0.3	7.03 ± 0.53	8.92 ± 1.05	< 0.001

Abbreviations: BMI, body mass index; DM, diabetes mellitus; DPN, diabetic peripheral neuropathy; RBS, random blood sugar.

median nerve. To ensure accurate measurements, the transducer was placed perpendicular to the nerve fibers, with minimal pressure applied to prevent nerve deformation and false measurements.

SWE images were obtained in the longitudinal view of the tibial and median nerves by rotating the probe 90 degrees from the transverse view. Stable SWE images were acquired after a brief stabilization period without movement.

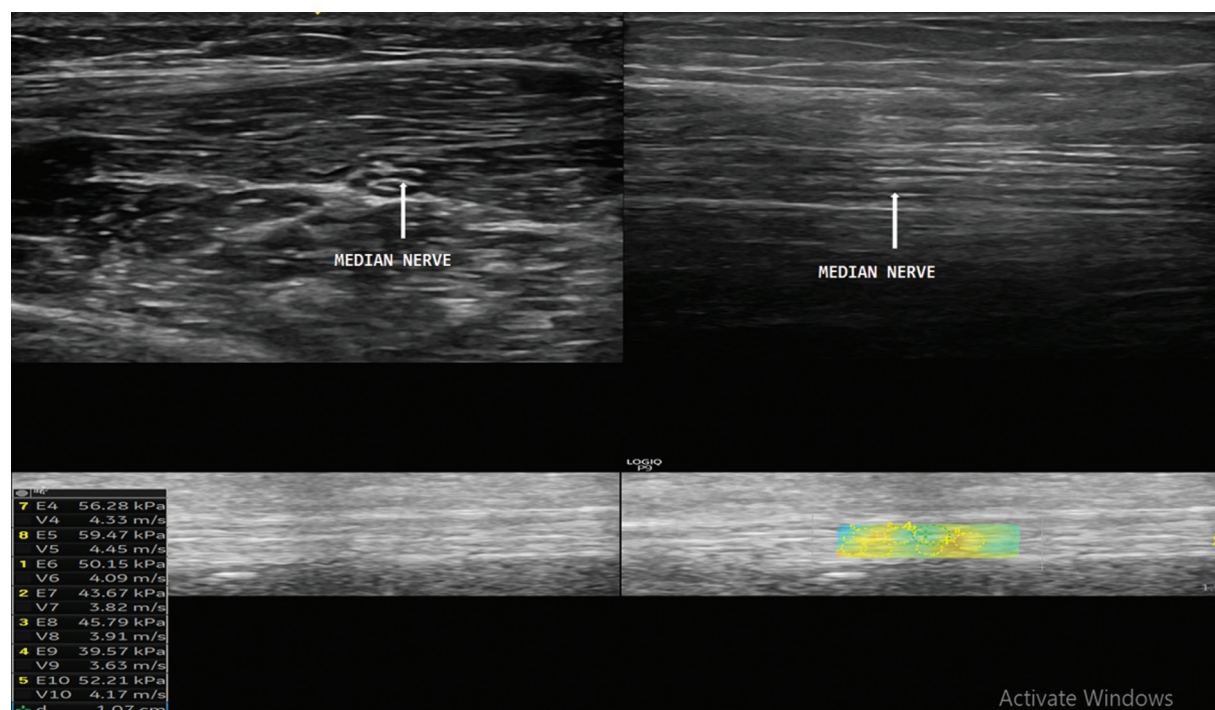
An automated circular region of interest (ROI) of fixed size of 2 mm<sup>2</sup> was positioned just inside the hyperechoic perineurium nerve border. Based on the SWE images, quantitative velocities of the tibial and median nerves were taken in meters per second (m/s) three times and then the mean of the three measurements was calculated for each nerve.

## Results

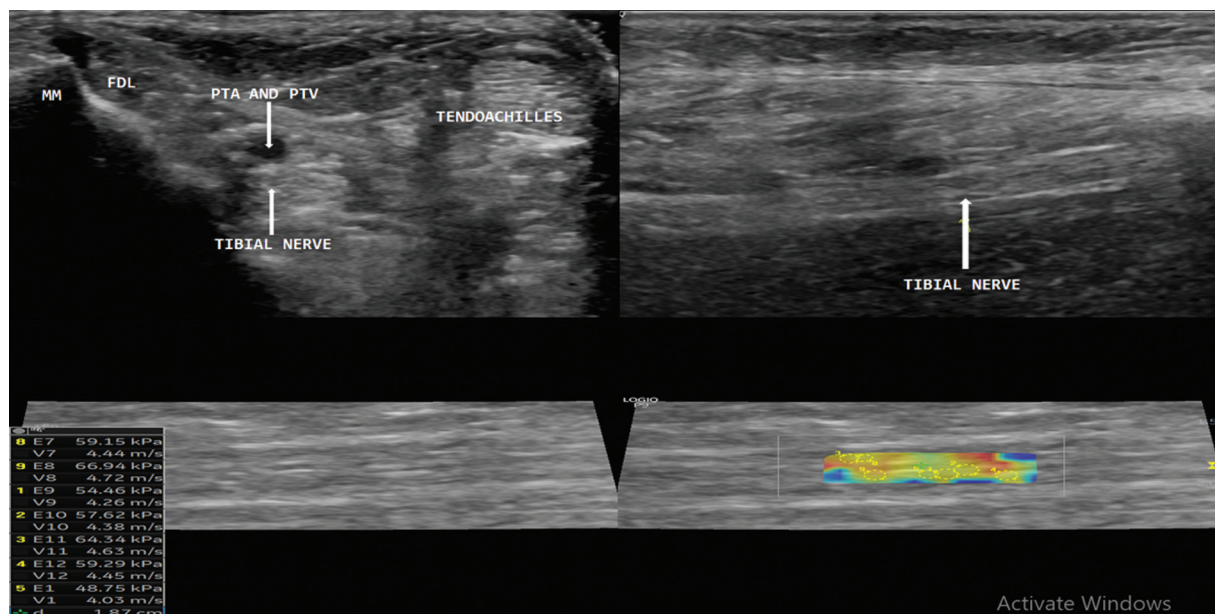
During the study period, 33 cases in the DM group with DPN, 33 cases of DM without DPN in the DPN group, and 34

healthy volunteers in the normal group were identified after applying the inclusion and exclusion criteria. The demographic characteristics, including age, gender, and body mass index (BMI), showed statistically significant differences among the examined groups ( $p < 0.001$ ). The mean age of the normal group was  $41.18 \pm 12.34$  years, while patients with DM and DPN had mean ages of  $46.30 \pm 20.30$  and  $50.24 \pm 13.00$  years, respectively. The HbA1c levels were highly significant in patients with DPN compared with those with DM ( $p < 0.001$ ; **Table 1**).

Both left and right tibial SWE values showed a significant increase from the normal group to the DM group and further increase in the DPN group ( $p < 0.001$  for all group comparisons). Similarly, both left and right median SWE values demonstrated a significant increase from the normal group to the DM group, and a further increase in the DPN group (**Figs. 1–4**;  $p < 0.001$  for all group comparisons), except for the comparison between the normal and DM groups for the right median SWE value, which showed significance at



**Fig. 1** In a diabetic patient with symptoms of peripheral neuropathy, the median nerve of the right upper limb (arrows) was observed in cross-sectional and longitudinal planes at the midpoint of the forearm. The stiffness (m/s) was generated, with the average value being taken as 4.23 m/s.

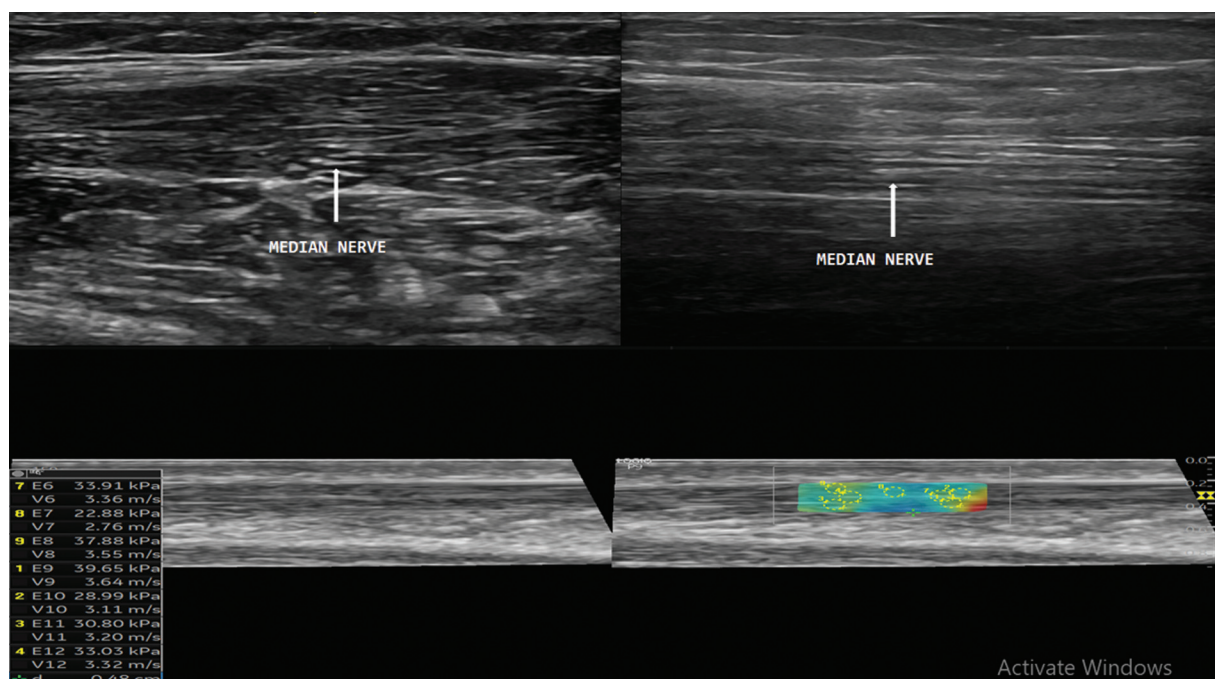


**Fig. 2** In a diabetic patient with symptoms of peripheral neuropathy, the tibial nerve of the left lower limb (arrows) was observed in cross-sectional and longitudinal planes 3 cm above the medial malleolus in the cross-sectional plane. The stiffness (m/s) was generated, with the average value being taken as 4.31 m/s. Abbreviations: cm, centimeter; m/s, meter per second.

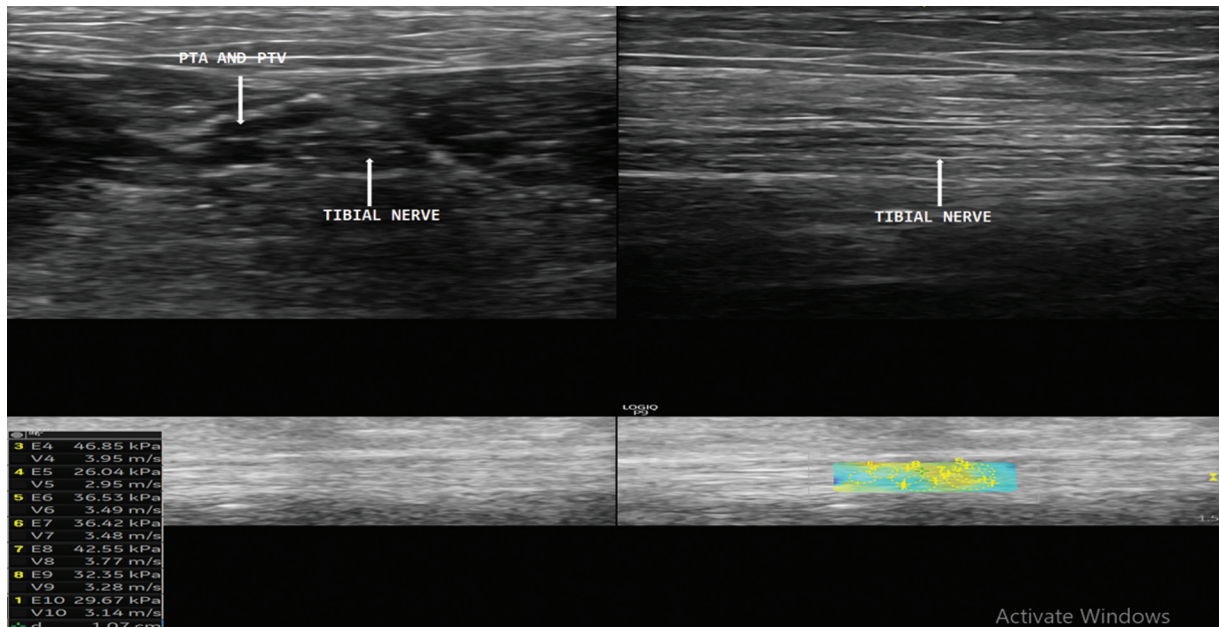
$p = 0.047$ . Overall, these findings indicate a progressive elevation in SWE values from normal to DM to DPN groups, highlighting the potential of SWE as a diagnostic tool for DPN (→Table 2).

The area under the curve (AUC) values for the SWE variables indicated their diagnostic accuracy in distinguishing DPN from non-DPN cases. The left and right tibial SWE values had AUCs of 0.979 and 0.985, respectively, indicating

excellent discrimination. Both showed 100% sensitivity and 97% specificity. The left median SWE value had an AUC of 0.989 with 93.9% sensitivity and 97% specificity, demonstrating outstanding discriminatory ability. The right median SWE value had an AUC of 0.953 with 100% sensitivity and 92.5% specificity, still showing excellent discriminatory power. All SWE variables significantly distinguished DPN from non-DPN cases ( $p < 0.001$ ), with less false-positive rates.



**Fig. 3** In a diabetic patient without symptoms of peripheral neuropathy, the median nerve of the left upper limb (arrows) was observed in cross-sectional and longitudinal planes at the midpoint of the forearm. The stiffness (m/s) was generated, with the average value being taken as 3.72 m/s.



**Fig. 4** In a healthy individual, the tibial nerve of the left lower limb (arrows) was observed in cross-sectional and longitudinal planes 3 cm above the medial malleolus in the cross-sectional plane. The stiffness (m/s) was generated, with the average value being taken as 3.68 m/s. Abbreviations: cm, centimeter; m/s, meter per second.

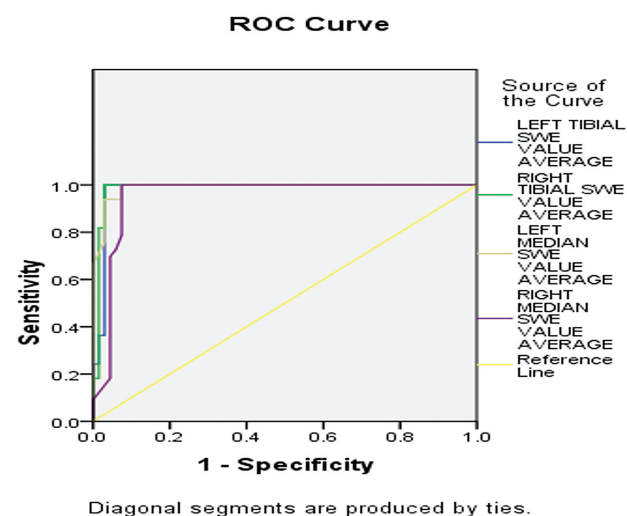
**Table 2** Mean SWE value of bilateral nerves among groups

SWE value average	Normal (n = 34), m/s	DM (n = 33), m/s	DPN (n = 33), m/s	p-value	Normal vs. DM	Normal vs. DPN	DM vs. DPN
Left tibial	3.63 ± 0.14	3.71 ± 0.03	4 ± 0.04	<0.001	<0.001	<0.001	<0.001
Right tibial	3.62 ± 0.14	3.7 ± 0.04	4 ± 0.05	<0.001	<0.001	<0.001	<0.001
Left median	3.61 ± 0.13	3.69 ± 0.04	3.95 ± 0.03	<0.001	<0.001	<0.001	<0.001
Right median	3.63 ± 0.17	3.7 ± 0.05	3.94 ± 0.05	<0.001	0.047	<0.001	<0.001

Abbreviations: DM, diabetes mellitus; DPN, diabetic peripheral neuropathy; SWE, shear wave elastography.

These findings underscore the utility of SWE in diagnosing DPN (→ Fig. 5). The analysis also revealed cutoff values of 3.902 and 3.897 m/s for the left and right tibial nerves,

respectively. Similarly, for the median nerve, the AUC values were 0.989 for the left median nerve and 0.953 for the right median nerve, both with a p-value of less than 0.001. These results indicate high diagnostic accuracy for detecting DPN using the median nerve SWE values. The analysis revealed cutoff values of 3.887 and 3.835 m/s for the left and right median nerves, respectively (→ Table 3).



**Fig. 5** Receiver operating characteristic (ROC) curve of bilateral nerves. SWE, shear wave elastography.

## Discussion

DPN poses a significant challenge in diagnosis due to the lack of well-defined ultrasonography criteria. However, ultrasound elastography offers a promising noninvasive method to quantify tissue stiffness objectively.

High-resolution ultrasound, particularly in neuromuscular contexts, provides detailed insights into nerve structure, facilitating the assessment of DPN severity.

SWE emerges as a valuable tool, measuring nerve stiffness by shear wave propagation velocity, which correlates with tissue hardness.

SWE utilizes transient pulses to create shear waves in tissues, measuring their stiffness via computer analysis. The resulting color-coded images offer a quick and precise

**Table 3** Area under the curve (AUC) analysis of shear wave elastography (SWE) of median and tibial nerves in patients among groups

Mean SWE of nerves	AUC	p-value	Cutoff value (m/s)
Left tibial nerve	0.979	<0.001	3.902
Right tibial nerve	0.985	<0.001	3.897
Left median nerve	0.989	<0.001	3.887
Right median nerve	0.953	<0.001	3.835

assessment of tissue stiffness, aiding health care professionals in diagnostics and treatment decisions.<sup>12</sup>

The emerging ultrasound technology, SWE, meets early DPN screening requirements because of its real-time capabilities, simplicity, noninvasiveness, and repeatability. Additionally, its functional assessment of nerves compensates for the limitations of traditional high-frequency ultrasound, providing unique advantages in the early recognition and diagnosis of DPN.<sup>13</sup>

Previous studies by Dikici et al<sup>14</sup> and Ishibashi et al<sup>15</sup> have demonstrated increased stiffness in the tibial nerve of DPN patients compared with controls. However, this study explores a novel approach, examining both the tibial and median nerves using SWE, revealing comparable stiffness between them in DPN patients. This suggests proximal nerve alterations in DPN, challenging traditional wrist-based median nerve assessments.

Additionally, there was a significant increase in nerve elasticity in diabetic patients without DPN compared with control subjects. These findings align with previous research by He Y et al.<sup>2</sup>

Despite the insightful findings, limitations exist. The study focuses on only two nerves, overlooking others affected by DPN. Furthermore, it does not explore the correlation between nerve stiffness and DPN severity, necessitating longitudinal studies. Finally, the inability to validate stiffness changes through histopathology underscores the need for further research to confirm these findings.

Jiang et al<sup>16</sup> discovered that in diabetic patients with DPN, the  $E_{\text{Mean}}$ ,  $E_{\text{Min}}$ , and  $E_{\text{Max}}$  values of the tibial nerve were notably larger compared with those in diabetic patients without DPN and normal control individuals. However, there was no significant statistical difference in nerve stiffness between diabetics without DPN and control individuals.

SWE represents a promising technique capable of indicating the stiffness of nerves by measuring the velocity of shear wave propagation. The speed of shear wave propagation increases with tissue hardness. Therefore, SWE offers the potential for a more quantitative evaluation of tissue stiffness.

In our study, the AUC values for the SWE variables (0.979 and 0.985, respectively) indicate their excellent diagnostic accuracy in distinguishing DPN from non-DPN cases. Both show 100% sensitivity and 97% specificity.

The right median SWE value has an AUC of 0.953, with 100% sensitivity and 92.5% specificity, still showing excellent discriminatory power. The same findings were observed by Elfattah Hassan Gadalla et al.<sup>17</sup> An 89% sensitivity and 100% specificity in the detection of DPN findings underscore the utility of SWE in diagnosing DPN.

SWE demonstrates promising diagnostic accuracy in detecting DPN. It holds considerable potential as a noninvasive adjunctive tool in managing patients with DPN.<sup>18</sup>

DPN reveals as a multifaceted neuropathy affecting the distal extremities. Presently, research on DPN ultrasound elastography primarily focuses on evaluating the elasticity of nerves in the lower limbs. What sets this study apart is its advanced approach of assessing the tibial nerve of the lower extremity using SWE, and analyzing the upper extremity's median nerve. The study compared the elastic values of the median nerve and tibial nerve in DPN patients and found no statistically significant difference between them. Additionally, unlike previous examinations that commonly selected the wrist as the measurement site for the median nerve, this study opted for a location in the middle of the forearm. The results indicated that nerve stiffness in the DPN group was higher than that in the DM group and the control group, suggesting proximal nerve alterations in DPN.

Several limitations persist in our study. First, DPN is a disorder affecting multiple peripheral nerves. While we examined the median nerve and tibial nerve, numerous other peripheral nerves and different segments of the same nerve should ideally be measured. For example, for the median nerve, measurements should be taken at the wrist, 2 cm proximal to the wrist crease, and at the elbow; for the tibial nerve, measurements should be taken at the popliteal fossa, and so forth. Additionally, our study did not delve into the detailed relationship between nerve stiffness and the severity of diabetic neuropathy. Longitudinal studies are required to elucidate temporal changes in nerve stiffness. Finally, we could not validate changes in DPN stiffness through histopathology due to the absence of nerve biopsies.

## Conclusion

The study concluded that shear wave ultrasound elastography of the tibial and median nerves is a noninvasive procedure with high sensitivity and specificity for detecting DPN. It revealed increased stiffness in the tibial and median nerves among individuals with DPN compared with those with DM and those in the control groups. Moreover, the study found that the diagnostic accuracy of DPN was improved by combining high-resolution ultrasound with complementary SWE of the tibial and median nerves. As a result, SWE emerges as a valuable adjunctive imaging method for detecting DPN.

## Note

Logic P9 ultrasound machine equipped with a high-frequency linear transducer (3–12 MHz) was used in this study.

**Funding**

None.

**Conflict of Interest**

None declared.

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